



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of **Goddard et al.** ) Examiner: Gyan Chandra  
Serial No. 10/735,014 ) Group Art Unit: 1646  
Filed: December 12, 2003 ) Attorney's Docket No. 10466/486  
Title: **SECRETED AND** )  
**TRANSMEMBRANE** )  
**POLYPEPTIDES AND NUCLEIC** )  
**ACIDS ENCODING THE SAME** )

**DECLARATION OF AUDREY GODDARD, Ph.D., PAUL J. GODOWSKI, Ph.D.,**  
**J. CHRISTOPHER GRIMALDI, AUSTIN L. GURNEY, Ph.D., DANIEL TUMAS, Ph.D.**  
**AND WILLIAM I. WOOD, Ph.D. UNDER 37 CFR § 1.131**

**MAIL STOP AMENDMENT**

The Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

We, Audrey Goddard, Ph.D., Paul J. Godowski, Ph.D., J. Christopher Grimaldi, Austin Gurney, Ph.D., Daniel Tumas, Ph.D. and William I. Wood, Ph.D. declare and say as follows:

1. We are the inventors of the above-identified application.

2. At the time the present invention was made, one of the inventors, Daniel Tumas, Ph.D., was responsible for overseeing the testing of novel polypeptides, including the polypeptide PRO361, in an assay of inhibitory activity in the mixed lymphocyte relation (MLR) (Assay #67, Example 34). This assay is used to find agents that are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

3. The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12, edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50:1 of irradiated stimulator cells, and

50:1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1x10<sup>7</sup> cells/ml of assay media. The assay is then conducted as described above.

Any decrease below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein. The results are indicative of the utility of the PRO polypeptides in therapeutic applications where suppression of an immune response is beneficial.

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4. Copies of pages from an internal database showing the positive results for the PRO361 polypeptide (SEQ ID NO: 83), identified by Pin number PIN996-1, in Assay #67 are attached to this declaration (with dates redacted) as Exhibit A. These experiments were performed and the results were obtained in the United States prior to August, 1999.

5. Exhibit A clearly shows that the polypeptide designated PRO361 was tested, and its ability to inhibit the mixed leukocyte reaction was determined prior to August, 1999.

6. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

A. Goddard  
Audrey Goddard, Ph.D.

1/12/08  
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Paul J. Godowski, Ph.D.

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Date

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J. Christopher Grimaldi

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Audrey Goddard, Ph.D.

*Paul J. Godowski*  
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Paul J. Godowski, Ph.D.

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Paul J. Godowski, Ph.D.

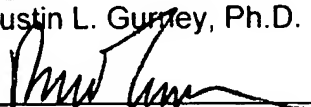
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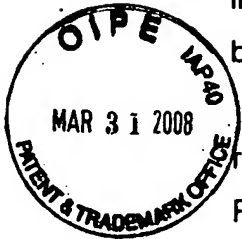
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Daniel Tumas, Ph.D.

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February 14, 2008  
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William I. Wood, Ph.D.

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Date



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J. Christopher Grimaldi

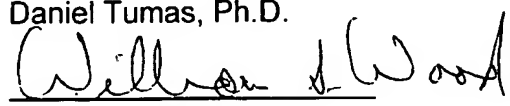
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## EXHIBIT A



GenesGenes Enter search terms



SEARCH REQUEST SYSTEMS ANALYSIS TOOLS HISTORICAL SPDI RECORD

Quick search: DNA Enter ID number

Assay Viewer  
SPDI A44895

AST517 Rat Photoreceptor Cell cAMP Synergy (2 Da)  
AST518 Rat DRG Neuronal Survival Inhibition Assay  
AST519 Ventralization of Xenopus Embryo by DNA  
AST560 Benzidine Staining of Xenopus Embryo by  
AST561 Ventralization of Xenopus Embryo by DNA  
AST562 Ventralization of Xenopus Embryo by DNA  
AST563 Neuroprotection of stem cell proliferation  
AST564 Proliferation/PNH Inhibition  
AST565 HUVEC Survival in Absence of Serum  
AST566 Inhibition of Apoptosis Differentiation  
AST567 MLK - Inhibition

Lot for Search

PH996-1

Show Lots for:  
LOT 102  
1178  
Include UNQ Related Lots

☐ All Positives ☐ Verified Positives ☐ Pending

Date Complete From

ASSAY RESULT LIST  
AST AST Name  
AST562 MLK-Inh  
AST562 MLK-Inh  
AST562 MLK-Inh  
AST562 MLK-Inh

Rows 1 - 4 of 4  
LOT LOT Name  
LOT102 PH996-1  
LOT102 PH996-1  
LOT102 PH996-1  
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Page 1 of 1  
Cons Conc Unit Mean Ctl  
1.50 nM 63.2  
1.50 nM 77.3  
15.00 nM 64.7  
15.00 nM 99.4

Select Page Page No. 1  
UNQ UNQ  
UNQ316 Human MAHSC1 IgG  
UNQ316 Human MAHSC1 IgG  
UNQ316 Human MAHSC1 IgG  
UNQ316 Human MAHSC1 IgG

Date Date Data Complete Comment

Meta | Feedback | Support  
GenesGenes is maintained by Bioinformatics